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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,453	10/22/2001	Brian G. Fox	09820.188	2389

7590 07/26/2004

Intellectual Property Department
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EXAMINER	
SAIDHA, TEKCHAND	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/001,453	FOX ET AL.	
	Examiner	Art Unit	
	Tekchand Saidha	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *23 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-15,17-25 and 27-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-15,17-25 and 27-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment and affidavit (rule 131 and 132) filed June 23, 2004, is acknowledged.

2. Claims 6, 16 & 26 have been cancelled and new claims 31-39 have been added by the amendment, cited above.

3. Accordingly, claims 1-5, 7-15, 17-25 & 27-39 are pending and under consideration in this examination.

3. ***Priority***

For prior art purposes, with no earlier claims to priority, the filing date of 10/22/01 for this application will be considered the priority date.

4. Any objection or rejection of record not expressly repeated in this Office Action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed as per the amendment cited above have been fully considered but they are not deemed to be persuasive or are moot in view of the new grounds of rejection. The reasons are discussed following the rejection(s).

6. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Written Description

Claims 1-5, 7-15, 17-25 & 27-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-5, 7-15, 17-25 & 27-39 are directed to labeled apo or holo or acylated acyl carrier protein from any source and wherein the non-radioactive label can be any fluorophore including dansyl, fluorescein, rhodamine, fluorescein isothiocyanate (FITC) or tetramethylrhodamine isothiocyanate (TRITC) & Texas Red; a kit and methods based thereof. Claims 1-5, 7-15, 17-25 & 27-39 are rejected under this section of 35 U.S.C. 112 because the claims are directed to a genus of labeled acyl carrier proteins (ACPs) obtained by numerous chemical modifications, kits and method thereof that are encompassed by the claims and for which no description is apparent. This is would include the genus of ACP from any source as well as the numerous chemical modifications or reactions that are not described. No description is provided of such ACPs and the numerous fluorophores each requiring different chemical reaction conditions to obtain labeled ACP encompassed by the claim. No information, beyond the labeling of different forms of *Escherichia coli* [apo or holo or acylated] acyl carrier protein comprising a 77 amino acid sequence [Abita et al. Eur. J. Biochem. 23 (1971) : 412-420, IDS] and having a single tyrosine residue, which is labeled by reacting the with dansyl chloride with the formation of DansylaminoTyr-ACP (and kit and methods of making) has been provided by applicants which would indicate that they had possession of the claimed genus of labeled ACPs by any fluorophore or wherein the fluorophore is selected from fluorescein, rhodamine, fluorescein isothiocyanate (FITC) or tetramethylrhodamine isothiocyanate (TRITC) & Texas Red, kits and methods of making. The specification does not contain any disclosure of the methods used in the labeling of all the numerous known or unknown carrier proteins with the diverse group of

fluorophores. The genus of ACPs and the fluorophores used in the product or method (or kit) claimed is a large variable genus including ACPs and chemical modifications using different fluorophore (or reactions) not described in the instant specification, wherein each of the fluorophores require a different set of conditions and react differentially. For example, using dansyl chloride and alkaline pH, amino acid tyrosine of the protein is reactive. Using Rhodamine Red require having a reactive succinimidyl ester moiety, which reacts with the primary amine of the proteins to form a stable dye-protein conjugate [See Molecular Probe Product No. F-6161 (Rhodamine Red), Applicants IDS filed June 23, 2004]. The specification discloses only selected *Escherichia coli* dansylated labeled product DansylaminoTyr-ACP as the species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Further, labeling of tyrosine by dansylation is known, however, in claims 8-9, 17-18, 27-28, 32-37 & 39 for example, Applicants' recite fluorophores such as fluorescein, rhodamine, fluorescein isothiocyanate (FITC) or tetramethylrhodamine isothiocyanate (TRITC) & Texas Red, which are not known or described in the instant specification to label tyrosine of the protein or covalently bonded to tyrosine as claimed. Further it is not a question of availability of different fluorophores or dyes or of different ACPs, it is the chemical reaction involved viz. dansylation, which is not representative of the all the other fluorophores. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicants' Arguments:

Applicants traverse the rejection for written description requirement for the same reasons articulated in the enablement section. Applicants further argue that 'while the enablement and written description requirements of § 112 are separate, they are closely related. Specifically addressing the written description requirement itself, Applicants traverse the rejection because defining a generic term by listing a number of exemplary species that fall within the generic term is a perfectly valid and approved approach to defining a generic term. See MPEP 2164.08 and In re Marzocchi, 169 USPQ 367, 370 (CCPA 1971): "How a teaching is set forth, by specific example or broad terminology, is not important. " (Emphasis added.) Moreover, what is well-known in the art is best omitted from the specification. MPEP j2164.08 and In re Buchner, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991). Further still, Applicants are not required to describe and test every single species falling within a generic claim. See In re Angstadt 190 USPQ 214 (CCPA 1976). The specification provides extensive written documentation of suitable ACPS, suitable non-radioactive labels, and how to affix the labels to the ACPS. By listing quite a large number of species falling within each respective genus ("ACP" and "non-radioactive label") Applicants submit that the specification complies with the written description requirement as per the guidelines in the MPEP and the controlling case law.

In response Applicants are referred to the 'Written Description Guidelines for Examination of Patent Application Under the 35 U.S.C. 112 [Federal Register, Vo. 66, No. 4, January 5, 2001], which provides the guidelines. According to these guidelines,

the written description requirement of the invention is separate and distinct from the enablement requirement. The essential goal of the description of the invention requirement is to clearly convey the information that an Applicant had invented the subject matter which is claimed. Another objective is to put the public in possession of what the Applicant claims as the invention. Therefore, Applicants arguments based case laws governing enablement [In re Marzocchi, 169 USPQ 367, 370 (CCPA 1971) & In re Buchner, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991)], are not quite relevant .

One of the ways of meeting the written description requirement is to shoe that the disclosed species is representative of the genus because the specification teaches sufficient common attributes of the elements possessed by the members of the genus. However, in the instant case, this is not so.

The application provides a single species in E. coli ACP having a single tyrosine at the carboxyl terminal which is dansylated and therefore useful as a tracer in fatty acid metabolism. Extrapolating dansylation of the tyrosine of the single species to includes any ACP protein [because ACP sequence are conserved] may well be representative of the genus. However, modifying any ACP protein by different fluorophores involving different reactions is not representative of the single described species, because apart from dansyl chloride, no other fluorophore has been described or exemplified, and dansyl chloride is not a species representative of the various fluorophores, because of the different reaction mechanisms. Therefore, the written description requirements are not met.

7. ***Claim Rejections - 35 USC § 112*** (second paragraph)

Claims 8-9, 17-18, 27-28, 32-37 & 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8-9, 17-18, 27-28, 32-37 & 39 recite or depend from a claim that recites labeling of tyrosine by fluorophores other than by dansylation. The claims are indefinite because the labeling of tyrosine by dansylation is known, however, fluorophores such as fluorescein, rhodamine, fluorescein isothiocyanate (FITC) or tetramethylrhodamine isothiocyanate (TRITC) & Texas Red, are not known to label tyrosine of the protein by covalent bonding.

8. Claim 19, has a typographical error in having a 'period' twice. Correction is required.

9. The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification or have an active link in an information disclosure statement (IDS) which references are published (for example, IDS filed June 23, 2004) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP 608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference.

10. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Rejection of claims 1-30 under 35 U.S.C. 102(a) as being anticipated by Haas et al. [**Protein Expression and Purification** Volume 20, Issue 2, November 2000, Pages 274-284] **is withdrawn** in view of the combined rule 131/132 declaration by the inventors of the instant application that the invention was conceived prior to November 1, 2000.

11. Claims 1-3, 7-10 & 17-18 are rejected under 35 U.S.C. 102(b) as being anticipated McAllister et al. [Abstracts of the Interscience Conference on Antimicrobial Agents and Chemotherapy, (2000) Vol. 40, pp. 225. print. Meeting Info.: 40th Interscience Conference on Antimicrobial Agents and Chemotherapy. Toronto, Ontario, Canada. September 17-20, 2000].

McAllister et al. teach the use of Fluorescein-labeled Co-enzyme A for the detection of acyl carrier protein synthase, which is labeled. The method is also used for the incorporation of Fluorescein-labeled Co-enzyme A into halo and apo-ACP, wherein incorporation of the label into apo-ACP was verified by mass spectrometry. The synthase as known in the art has at least one tyrosine. The labeled ACPs of the

reference are no different than that claimed, irrespective of the method of making it. The reference therefore anticipates the claims.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-5, 11-15, 19-25 & 27-39 rejected under 35 U.S.C. 103(a) as being unpatentable over McAllister et al. (2000), Abita et al. [Eur. J. Biochem. 23 (1971) : 412-420, IDS], Dawson et al. [Data for biochemical research, 3rd edition, 1986, see reagents for protein modifications, pages 388-393] and any of the Molecular Probes FluoReporter kits comprising : Rhodamine Red, Texa Red, Fluorescein or FITC [IDS filed June 23, 2004].

The teachings of McAllister et al. are described above in the foregoing paragraph. McAllister et al. do not teach ACP from *E.coli* or the use of other fluorophores such as dansyl [chloride], rhodamine, fluorescein isothiocyanate (FITC) or tetramethylrhodamine isothiocyanate (TRITC) & Texas Red. No kits comprising ACP and the fluorophores, or method of making the fluorophores-ACP complex are described.

Abita et al. teach *Escherichia coli* apo or holo or acylated acyl carrier protein comprising a 77 amino acid sequence and having at least one tyrosine residue. Abita et al. do not teach labeling of the *E. coli* ACP with a fluorophore, as a non-radioactive label.

Dawson et al. (1986) teach a number of reagents for protein modifications including Dansyl chloride, FITC (I & II) and Rhodamine B, detailing the method(s) in the references cited therein. Similarly, a number of FluoReporters: Rhodamine Red, Texa Red, Fluorescein or FITC are available in protein labeling kits from Molecular Probes. These methods are general methods applicable to labeling any protein. The references do not specifically teach the labeling of the ACP proteins.

Based upon the teachings of the prior art references cited here, it would have been obvious to one of ordinary skill in the art to extend the teachings of McAllister by fluorophore labeling Acyl Carrier Protein Synthase to include any of the well known and widely available reagents in Molecular Probes or that taught by Dawson et al., or in the alternative substitute the Synthase with the *E. coli* ACPs taught by Abita et al., and do so with a reasonable expectation of success. The combined teachings also lay clear and obvious guidelines into developing method(s) or kit(s) that would encompass the claims under prosecution. One of ordinary skill in the art would have been motivated in view of the non-invasive nature of the label as opposed to radio-active label used *in-vivo* or *in-vitro* methods; or for greater convenience for the detection of ACP-synthase (AcpS) activity without using radioactive CoA derivative as suggested by McAllister et al. Barring any unpredictable results and non seems to have been reported here, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272

0940. The examiner can normally be reached on Monday-Friday, between 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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